



## Selective and efficient synthesis of di-, tri- and tetrasubstituted 1,10-phenanthrolines

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**Abstract:** A general synthetic procedure for the preparation of multisubstituted phenanthrolines is presented. Bromination of 1,10-phenanthroline at the 3 and 8 positions, followed by Suzuki coupling reaction and subsequent methylation afford the di-, tri and tetra- substituted phenanthrolines in good yields. These phenanthroline derivatives are useful building blocks in the construction of highly sophisticated molecular architectures.  
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**Keywords:** 1,10-phenanthroline; Suzuki coupling; disymmetric functionalization.

The chemistry of classical chelates such as 2,2'-bipyridine, 1,10-phenanthroline and 2,2',6',2''-terpyridine has undergone an explosive development in the last two decades, in parallel with coordination chemistry. The construction of highly sophisticated molecular architectures incorporating various transition metal complexes<sup>1–6</sup> relies most of the time on multifunctional ligands incorporating several coordination sites. In the course of the elaboration of such compounds, it is essential to have at disposal synthetic methods leading to high-yield synthesis of chelates bearing various substituents at appropriate positions. We would now like to report new synthetic procedures which allow to prepare in good yield multisubstituted 1,10-phenanthrolines including, in particular, *disymmetrical compounds* bearing various groups at the 2,9 and 3, 8 positions.

Our approach towards the multisubstituted phenanthrolines (represented in Figure 1) relies on two types of C-C bond formation. It takes advantage of the easy access to 3,8-dibromo-1,10-phenanthroline, as recently reported.<sup>7</sup> 1,10-Phenanthroline was treated with Br<sub>2</sub> in the presence of S<sub>2</sub>Cl<sub>2</sub> and pyridine in 1-chlorobutane to afford 3,8-dibromo-1,10-phenanthroline (**1**) in 75 % yield. Reaction of **1** with 2.2 equivalents of the ester of *p*-methoxyphenylboronic or *p*-fluorophenylboronic acids under Suzuki cross-coupling conditions<sup>8</sup> (Pd[P(C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>]<sub>4</sub> in toluene, aqueous Na<sub>2</sub>CO<sub>3</sub>, 80 °C, 12 h), afforded the 3,8-disubstituted derivatives **2a** and **2b** respectively. After cooling, **2a** and **2b** crystallized from the crude and thus they could be easily separated by filtration over a sintered disc filter funnel. Simultaneous introduction of the methyl groups in positions 2 and 9 of the phenanthroline nucleus was first tried at room temperature with an excess of CH<sub>3</sub>Li, but it led to **4a** or **4b** in very poor yield (~ 20 %). This yield could be largely improved by the two-step procedure depicted in Figure 1 (monosubstitution conditions: small excess of CH<sub>3</sub>Li and temperature maintained between 0 and 5 °C)<sup>9</sup>. These two successive monosubstitutions are not only beneficial in terms of yield, but may also give easily access to various *disymmetrical* 2,9-disubstituted phenanthrolines. In particular, **3a** or **3b** should easily undergo further

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addition of an alkyl or aryl group at the 9 position if needed.  $^1\text{H}$ -NMR and Mass Spectra were all in full agreement with the proposed structures for **2a-4b**.<sup>10</sup>

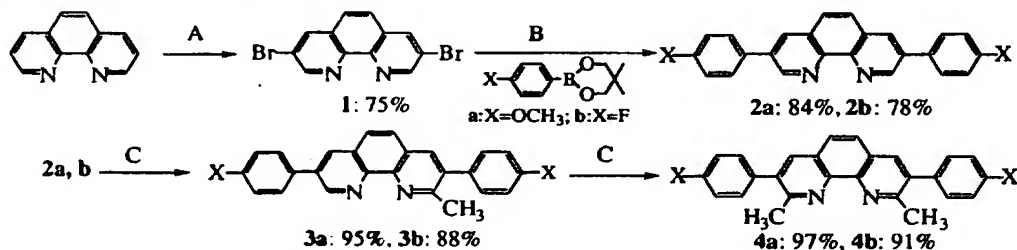


Figure 1

In conclusion, the present synthetic approach extends the family of preparative tools for making multisubstituted 1,10-phenanthrolines and thus complements other recently reported strategies.<sup>11-15</sup>

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- Melting points ( $^\circ\text{C}$ , uncorrected),  $^1\text{H}$ -NMR (200 MHz,  $\text{CDCl}_3$ ,  $\delta$  (ppm),  $J$  (Hz)) and MS (e.i.,  $M^+$  ( $m/z$ )) data: **2a**: m.p.: 271-273;  $^1\text{H}$ -NMR: 3.90 (s, 6H), 7.08 (d, 4H,  $J = 8.8$ ), 7.72 (d, 4H,  $J = 8.8$ ), 7.83 (s, 2H), 8.32 (d, 2H,  $J = 2.3$ ), 9.40 (d, 2H,  $J = 2.3$ ); MS: 392. **2b**: m.p.: 264-266;  $^1\text{H}$ -NMR: 7.26 (m, 4H), 7.76 (m, 4H), 7.90 (s, 2H), 8.38 (d, 2H,  $J = 2.3$ ), 9.41 (d, 2H,  $J = 2.3$ ); MS: 368. **3a**: m.p.: 242-244;  $^1\text{H}$ -NMR: 2.89 (s, 3H), 3.88 (s, 6H), 7.05 (m, 4H), 7.40 (d, 2H,  $J = 8.7$ ), 7.70 (d, 2H,  $J = 8.8$ ), 7.74 (s, 2H), 7.99 (s, 1H), 8.28 (d, 1H,  $J = 2.3$ ), 9.42 (d, 1H,  $J = 2.3$ ); MS: 406. **3b**: m.p.: 234-236;  $^1\text{H}$ -NMR: 2.89 (s, 3H), 7.24 (m, 4H), 7.44 (m, 2H), 7.76 (m, 2H), 7.83 (s, 2H), 8.06 (s, 1H), 8.38 (d, 1H,  $J = 2.1$ ), 9.44 (d, 1H,  $J = 2.1$ ); MS: 382. **4a**: m.p.: 251-252;  $^1\text{H}$ -NMR: 2.91 (s, 6H), 3.91 (s, 6H), 7.04 (d, 4H,  $J = 8.8$ ), 7.41 (d, 4H,  $J = 8.8$ ), 7.74 (s, 2H), 8.04 (s, 2H); MS: 420. **4b**: m.p.: 235-237;  $^1\text{H}$ -NMR: 2.88 (s, 6H), 7.21 (m, 4H), 7.44 (m, 4H), 7.76 (s, 2H), 8.05 (s, 2H); MS: 396.
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